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**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(Use as many sheets as necessary)

Complete if Known

Application Number	08/234,208
Filing Date	January 20, 1998
First Named Inventor	Coharty
Art Unit	1842
Examiner Name	Anne Holleran
Attorney Docket Number	49921-1

Examiner Initials*	Cite No. ¹	Document Number		Publication Date MM-QD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number/Kind Code ² (if known)	Number/Kind Code ² (if known)			
SEA	C105	US-6,541,214		04-01-2003	Cinton et al.	
	C106	US-20030056883		03-17-2003	Cinton et al.	
	C107	US-20040027788		02-05-2004	Cinton et al.	
	C108	US-20040032786		03-18-2004	Cinton et al.	
	C109	US-5,705,167		01-08-1998	Greene et al.	
	C110	US-5,811,086		09-22-1998	Ploeman et al.	
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Examiner Initials*	Cite No. ¹	Foreign Patent Document		Publication Date MM-QD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T*
		Country Code ³ Number ⁴ Kind Code ⁵ (if known)	Country Code ³ Number ⁴ Kind Code ⁵ (if known)				
SEA	C111	WO0028688		05-26-2000	Oregon Health Sciences University		
	C112	WO0044403		09-03-2000	Oregon Health Sciences University		
	C113	WO0181356		08-23-2001	Oregon Health Sciences University		
	C114	WO0214470		02-21-2002	Oregon Health and Science University		
	C115	WO05018988		02-24-05	Receptor BioLogix, Inc.		

Examiner Signature	<i>[Signature]</i>	Date	7/23/06
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Substitute for form 1449PTO		Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(Use as many sheets as necessary)</i>		Application Number	08/234,208
		Filing Date	January 20, 1999
		First Named Inventor	Doherty
		Art Unit	1842
		Examiner Name	Anne Holleran
		Attorney Docket Number	49321-1
Sheet	2	of	5

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ²
gu	C116	BAASNER et al., Reversible tumorigenesis in mice by conditional expression of the HER2/c-erbB2 receptor tyrosine kinase, <i>Oncogene</i> 13(5):901-11, 1996	
	C117	BOWIE et al., Deciphering the Message in Protein Sequences: Tolerance to Amino Acid Substitutions, <i>Science</i> 247:1306-1310, 1990	
	C118	BRANDON et al., Estrogen Receptor Gene Expression in Human Uterine Leiomyomata, <i>J. Clin. Endocrinol. Metab.</i> 80(6):1876-1881, 1995	
	C119	BRANDON et al., Progesterone receptor messenger ribonucleic acid and protein are overexpressed in human uterine leiomyomas, <i>Am. J. Obstet. Gynecol.</i> 168(1):78-85, 1993	
	C120	BRODOWICZ et al., Soluble HER-2/neu neutralizes biologic effects of anti-HER-2/neu antibody on breast cancer cells <i>in vitro</i> , <i>Int. J. Cancer</i> 73:875-879, 1997	
	C121	BROWN et al., Antibodies against Highly Conserved Sites in the Epidermal Growth Factor Receptor Tyrosine Kinase Domain as Probes for Structure and Function, <i>Biochem</i> 32:4659-4664, 1993	
	C122	BURGESS et al., Possible Dissociation of the Heparin-binding and Mitogenic Activities of Heparin-binding (Acidic Fibroblast) Growth Factor-1 from its Receptor-binding Activities by Site-directed Mutagenesis of a Single Lysine Residue, <i>J. Cell Biol.</i> 111:2129-2138, 1990	
	C123	CLINTON and BROWN, Generation and Use of Anti-peptide Antibodies Directed against Catalytic Domain of Protein Kinases, <i>Methods in Enzymol.</i> 200:463-474, 1991	
	C124	CLINTON and HUA, Estrogen action in human ovarian cancer, <i>Crit. Rev. Oncol/Hematol.</i> 25:1-9, 1997	
cl	C125	CLINTON et al., Estrogens increase the expression of fibulin-1, an extracellular matrix protein secreted by human ovarian cancer cells, <i>Proc. Natl. Acad. Sci. USA</i> 93:316-320, 1996	

SEA 1628029v1 49321-1
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GU	C128	DERMER, Another Anniversary for the War on Cancer, BioTechnology 12:320, 1994	
	C127	DI FIORE et al., <i>erbB-2</i> is a Potent Oncogene When Overexpressed in NIH/3T3 Cells, Science 237:178-182, 1987	
	C128	DILLMAN, Antibodies as Cytotoxic Therapy, J. Clin. Oncol. 12(7):1497-1515, 1994	
	C129	DOHERTY et al., An Alternative <i>HER-2/neu</i> Transcript of 8 kb Has an Extended 3'UTR and Displays Increased Stability in SKOV-3 Ovarian Carcinoma Cells, Gynecol. Oncol. 74:408-415, 1999	
	C130	DOUGALL et al., The <i>neu</i> -oncogene: signal transduction pathways, transformation mechanisms and evolving therapies, Oncogene 9:2109-2123, 1994	
	C131	GREENSPAN and DI CERA, Defining epitopes: It's not as easy as it seems, Nature Biotechn. 17:935-937, 1999	
	C132	HUA et al., SKOV3 Ovarian Carcinoma Cells Have Functional Estrogen Receptor but are Growth-resistant to Estrogen and antiestrogens, J. Steroid Biochem. Molec. Biol. 55(3/4):279-288, 1995	
	C133	HUDZIAK et al., Increased expression of the putative growth factor receptor <i>p185^{HER2}</i> causes transformation and tumorigenesis of NIH 3T3 cells, Proc. Natl. Acad. Sci. USA 84:7159-7163, 1987	
	C134	HYNES and STERN, The biology of <i>erbB-2/neu/HER-2</i> and its role in cancer, Biochimica et Biophysica Acta 1198:165-184, 1994	
	C135	JHASVALA-ROMERO et al., Herstatin inhibits heregulin-mediated breast cancer cell growth and overcomes tamoxifen resistance in breast cancer cells that overexpress <i>HER-2</i> , Oncogene 22:8178-8186, 2003	
	C136	JUSTMAN and CLINTON, Herstatin, an Autoinhibitor of the Human epidermal Growth Factor Receptor 2 Tyrosine Kinase, Modulates Epidermal Growth Factor Signaling Pathways Resulting in Growth Arrest, J. Biol. Chem. 277(23):20618-20624, 2002	
	C137	KERN et al., Inhibition of Human Lung Cancer Cell Line Growth by an Anti- <i>p185^{HER2}</i> Antibody, Am. J. Respir. Cell Mol. Biol. 9:448-454, 1993	
	C138	LAZAR et al., Transforming Growth Factor α : Mutation of Aspartic Acid 47 and Leucine 48 Results in Different Biological Activities, Mol. Cell. Biol. 8(3):1247-1252, 1988	
	C139	LEE and CLINTON, Serum Tyrosine Kinase Activity and Neoplastic Disease: Recent Results Cancer Res. 113:32-40, 1989	
	C140	LEWIS et al., Differential responses of human tumor cell lines to anti- <i>p185^{HER2}</i> monoclonal antibodies, Cancer Immunol. Immunother 37:255-263, 1993	

SEA 1628029v1 4932(-)
Scaris

3

cu	C141	LIN and CLINTON, A soluble protein related to the HER-2 proto-oncogene product is released from human breast carcinoma cells, <i>Oncogene</i> 8(4):639-643, 1991	
	C142	LIN and CLINTON, Human prostatic acid phosphatase has phosphotyrosyl protein phosphatase activity, <i>Biochem. J.</i> 235:351-357, 1986	
	C143	LIN and Clinton, The Epidermal Growth Factor Receptor from Prostate Cells is Dephosphorylated by a Prostate-Specific Phosphotyrosyl Phosphatase, <i>Mol. Cell Biol.</i> 8(12): 5477-5485, 1988	
	C144	LIN et al., Characterization of Tyrosyl Kinase Activity in Human Serum, <i>J. Biol. Chem.</i> 260(3): 1582-1587, 1985	
	C145	LIN et al., Developmental Expression of Tyrosyl Kinase Activity in Human Serum, <i>Human Biol.</i> 56(3):549-556, 1987	
	C146	LIN et al., Disulfide-Linked and Noncovalent Dimers of p185 ^{HER-2} in Human Breast Carcinoma Cells, <i>J. Cell. Biochem.</i> 49:290-295, 1992	
	C147	LIN et al., Insulin and epidermal growth factor stimulate phosphorylation of p185 ^{HER-2} in the breast carcinoma cell line, BT474, <i>Mol. Cell Endocrinol.</i> 68(2-3):111-118, 1990	
	C148	LIN et al., Tyrosyl Kinase Activity is Inversely Related to Prostatic Acid Phosphatase Activity in Two Human Prostate Carcinoma Cell Lines, <i>Mol. Cell Biol.</i> 8(12): 4753-4757, 1988	
	C149	LIU et al., MCF-7 breast cancer cells overexpressing transfected c-erbB-2 have an <i>in vitro</i> growth advantage in estrogen-depleted conditions and reduced estrogen-dependence and tamoxifen-sensitivity <i>in vivo</i> , <i>Breast Cancer Res. Treatment</i> 34:97-117, 1986	
	C150	MOLINA et al., NH ₂ -terminal Truncated HER-2 Protein but not Full-Length Receptor is Associated with Nodal Metastasis in Human Breast Cancer, <i>Clin. Cancer Res.</i> 8:347-353, 2002	
	C151	NATALI et al., Expression of the p185 encoded by HER2 oncogene in normal and transformed human tissues, <i>Int. J. Cancer</i> 45:457-461, 1990	
	C152	O'ROURKE et al., Trans receptor inhibition of human glioblastoma cells by erbB family ectodomains, <i>Proc. Natl. Acad. Sci. USA</i> 94:3250-3255, 1997	
	C153	PIETRAS et al., HER-2 tyrosine kinase pathway targets estrogen receptor and promotes hormone-independent growth in human breast cancer cells, <i>Oncogene</i> 10:2435-2446, 1995	
	C154	SEVERINO et al., Rapid loss of oestrogen and progesterone receptors in human leiomyoma and myometrial explant cultures, <i>Mol. Human Repro.</i> 2(11):823-828, 1996	
✓	C155	SHAMIEH et al., Receptor binding specificities of Herstatin and its Intron 8-encoded domain, <i>FEBS Letters</i> 568:163-168, 2004	

J. Lin 7/23/05

SEA 1628029v1 49321-1
Seattle

C156	SHEPARD et al., Monoclonal antibody Therapy of Human Cancer: Taking the HER2 Protooncogene to the Clinic, J. Clin. Immunol. 11(3):117-127, 1991
C157	STAVEROSKY et al., Herstatin, an autoinhibitor of the epidermal growth factor receptor family, blocks the intracranial growth of glioblastoma, Clin. Cancer Res. 11(1):335-40, 2005
C158	TZAHAR et al., Bivalence of EGF-like ligands drives the ErbB signaling network, EMBO Journal 16(16):4938-4950, 1997
C159	Uniprot Data base, Database accession No. ERB2_HUMAN, "Receptor tyrosine-protein kinase erbB-2 precursor," 8/13/87, www.ebi.uniprot.org/uniprot-srv/uniProtView.do?proteinID=ERB2_HUMAN&pager.offset=null
C160	XIA et al., Combination of EGFR, HER-2/neu, and HER-3 is a Stronger Predictor for the Outcome of Oral Squamous Cell Carcinoma Than Any Individual Family Members, Clin. Cancer Res. 5:4164-4174, 1999

Examiner Signature		Date Considered	7/23/05
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Sheet	1	of	1
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Complete # Known

Application Number	09/234,208
Filing Date	January 20, 1999
First Named Inventor	Doherty
Art Unit	1842
Examiner Name	Susan Ungar
Attorney Docket Number	48321-1

U.S. PATENT DOCUMENTS

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FOREIGN PATENT DOCUMENTS

FOREIGN PATENT DOCUMENTS						
Examiner (WDS)	Cite No.	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patenter or Applicant of Used Document	Pages, Columns, Lines, Where Relevant Passages Or Relevant Figures Appear	T ¹
		Country Code ² Number ³ Kind Code ⁴ # (Invent)				
JK	C113	WO0101354	08-23-2001	Oregon Health Sciences University		
J	C115	WO0601808	02-24-05	Receptor Biologics, Inc.		

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